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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,990	01/04/2005	Nicoletta Bianchi	Q85654	3209

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,990	BIANCHI ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of species rapamycin, and hydroxy urea in the reply filed on 12/22/06 was acknowledged and the traversal arguments were answered in the non-office action dated 2/6/07.

Applicant's amendment to claims in the response filed on 8/6/07 has been acknowledged.

Claims 1-4 are pending.

Claims 1-4 are examined on the merit.

Any objections and rejections made in the previous office action dated 2/6/07 and not specifically mentioned here are considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 1 remain rejected under 35 U.S.C. 102(a) as being anticipated by Johnston, et al., Blood, 98, 410.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Johnston, et al., Blood, 2001, 98, 410 in view of Rachmilewitz, British Journal of Haematology, 1995, 91, 263 -268.

In the instant application, applicants claim a method of treating [3-thalassaemia comprising administering a medicament comprising a pharmaceutically effective amount of rapamycin or a structural analog thereof to a patient in need of such treatment. The method wherein the rapamycin or the structural analog is in combination with at least one modifier of a transcription process selected from the group consisting of cytosine arabinoside, retinoic acid, plicamycin, mithramycin, hydroxyurea, guanine, guanosine, triphosphate (GTP), gaunosine diphosphate (GDP) and guanosine monophosphate (GMP).

Applicants have addressed the rejection of claim 1 under 35 USC 102(a) and rejection of claims 1-4 under 35 USC 103(a) together in their remarks filed on 8/6/07. Therefore, the response to the arguments below is towards applicant's remarks towards aforementioned rejections.

Applicants argue that "[T]he subject matter of Applicants' application is directed to induction of HbF. It is submitted that the subject matter of claim 1 is novel and therefore patentable over the art of record because rapamycin induces the expression of HbF in human erythroid cells from beta- thalassaemia patients" (page 3, last paragraph).

Applicants further state that, "[T]here is no teaching by Johnston et al. (Blood, 98, 410) that rapamycin would be beneficial to thalassaemic patients as HbF inducer. Rapamycin is presumably needed only in AAV-treated patients in order to induce the expression of the transgene in a controlled fashion" (page 5, last paragraph).

Applicants also state that, "[U]nlike the approach described by Johnston et al. (Blood, 98, 41Q.)., the present invention demonstrates that rapamycin retains a novel and unpredictable effect, which is the induction of HbF in beta-thalassaemic cells not treated with gene therapy vectors or other inducers. This activity of rapamycin occurs in the absence of transfection with AAV-based DNA, is unexpected, and allows including rapamycin within the list of HbF inducers" (page 5, last paragraph).

Applicant's arguments filed 8/6/07 have been fully considered but they are not persuasive because, the claim 1 has been drawn to a method of treating beta-thalassaemia comprising administering a medicament comprising a pharmaceutically effective amount of rapamycin or a

structural analog thereof to a patient in need of such treatment. The claim 1 as drawn does not recite that the claims are directed to induction of HbF. Therefore, applicants are arguing limitations that are not present in the claims as recited. Johnston, et al., anticipates claim 1 as recited as stated in our office action (page 3) dated 2/6/07. Note that applicants acknowledge that Johnston, "demonstrated that rapamycin, combined with injection of AAV vectors expressing EPOunder rapamycin control improved anemia in mouse model of thalassaemia". Thus the reference of Johnston, teaches treatment of beta-thalassaemia using rapamycin. Thus meets the limitation of the instant claim 1.

The cited reference of Rachmilewitz teaches that HU reagent has been reported to be efficacious in patients with sickle-13-thalassaemia (page 265, column 1, paragraph 1). The reference also teaches that therapies based on the modulation of existing gene expression, **given alone or in combination with other therapies**, appear to offer significant promise in favorably modifying the clinical course of patients with sickle-cell disease and β-thalassaemia (page 266, column 2, paragraph 2) as stated in the office action dated 2/6/07. Therefore, combination of references Johnston and Rachmilewitz., teaches the instant invention and hence the invention as a whole is obvious to one of ordinary skill in the art at the time the invention was made.

Therefore, the claim rejections under 35 USC 102(a) and 103(a) are appropriate and maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 4 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 recites the limitation "modifier of transcription process" in line 3. There is insufficient antecedent basis for this limitation in the claim. The claim as amended does not overcome the lack of antecedent basis limitation as stated in the office action dated 2/6/07.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R. Gudibande, Ph.D./
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Art Unit 1654

/ANISH GUPTA/
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PRIMARY EXAMINER